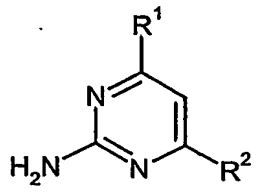
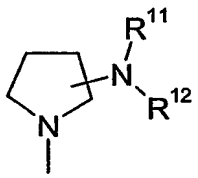
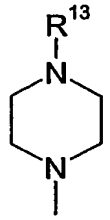
CLAIMS

1. A 2-aminopyrimidine derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof:



(I)

wherein

R^1 is  or  ,

wherein

R^{11} and R^{12} independently represent hydrogen or C_{1-6}alkyl optionally substituted by halogen, cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or C_{3-8}cycloalkyl;

R^{13} is C_{1-6}alkyl optionally substituted by halogen, cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or C_{3-8}cycloalkyl; and

R^2 is phenyl or naphthyl,

wherein

said phenyl and naphthyl are optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, cyano, hydroxy, nitro, phenyl, C_{1-6}-alkanoyl, N-(C_{1-6}alkyl)sulfonylamino, N-phenylsulfonylamino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, N-(C_{1-6}-alkoxycabonyl)amino, N-arylamino, N-(aryl C_{1-6}alkyl)amino, aminocarbonyl, N-(C_{1-6}-alkyl)aminocarbonyl, N,N-di(C_{1-6}alkyl)aminocarbonyl, C_{3-8}cycloalkyl, C_{1-6}alkyl-sulfonyl, sulfamoyl, aryl C_{1-6}alkoxycarbonyl, C_{1-6}alkyl, C_{1-6}alkyl substituted by cyano,

hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or mono-, di-, or tri- halogen, C_{1-6}alkoxy, C_{1-6}alkoxy substituted by mono-, di-, or tri- halogen, $-N(R^{21})C(O)N(R^{22})(R^{23})$, and $-N(R^{21})C(O)R^{24}$,

wherein

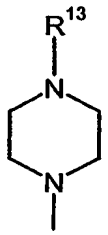
R^{21} is hydrogen or C_{1-6}alkyl;

R^{22} is C_{1-6}alkyl, or phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen;

R^{23} is hydrogen or C_{1-6}alkyl;

R^{24} is phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen.

with the proviso that when R^1 is



,

R^2 is optionally substituted phenyl, said phenyl is substituted by at least one substituent selected from the group consisting of carboxy, cyano, hydroxy, phenyl, C_{1-6}alkanoyl, N-phenylsulfonylamino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, N-(C_{1-6}alkoxycabonyl)amino, N-arylamino, N-(aryl C_{1-6}alkyl)amino, aminocarbonyl, N-(C_{1-6}alkyl)aminocarbonyl, N,N-di(C_{1-6}alkyl)aminocarbonyl, C_{3-8}cycloalkyl, C_{1-6}alkylsulfonyl, aryl C_{1-6}alkoxycarbonyl, C_{1-6}alkyl substituted by cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio,

C_{1-6}alkoxy, or mono-, di-, or tri- halogen, C_{1-6}alkoxy substituted by mono-, di-, or tri- halogen, $-N(R^{21})C(O)N(R^{22})(R^{23})$, and $-N(R^{21})C(O)R^{24}$,

wherein

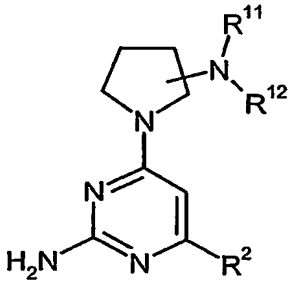
R^{21} is hydrogen or C_{1-6}alkyl;

R^{22} is C_{1-6}alkyl, or phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri-halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen;

R^{23} is hydrogen or C_{1-6}alkyl;

R^{24} is phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen.

2. A 2-aminopyrimidine derivative of the formula (I-i), its tautomeric or stereoisomeric form, or a salt,



(I-i)

wherein

R^{11} and R^{12} independently represent hydrogen or C_{1-6}alkyl optionally substituted by halogen, cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or C_{3-8}cycloalkyl; and

R^2 is phenyl or naphthyl,

wherein

said phenyl and naphthyl are optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, cyano, hydroxy, nitro, phenyl, C_{1-6}-alkanoyl, N-(C_{1-6}alkyl)sulfonylamino, N-phenylsulfonylamino C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, N-(C_{1-6}-alkoxycabonyl)amino, N-arylamino, N-(arylC_{1-6}alkyl)amino, aminocarbonyl, N-(C_{1-6}-alkyl)aminocarbonyl, N,N-di(C_{1-6}alkyl)aminocarbonyl, C_{3-8}cycloalkyl, C_{1-6}alkyl-sulfonyl, sulfamoyl, aryl C_{1-6}alkoxycarbonyl, C_{1-6}alkyl substituted by cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or mono-, di-, or tri- halogen, C_{1-6}alkoxy optionally substituted by mono-, di-, or tri-halogen, $N(R^{21})C(O)N(R^{22})(R^{23})$, and $N(R^{21})C(O)R^{24}$,

wherein

R^{21} is hydrogen or C_{1-6}alkyl;

R^{22} is C_{1-6}alkyl, or phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono- di-, or tri- halogen;

R^{23} is hydrogen or C_{1-6}alkyl; and

R^{24} is phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen.

3. The 2-aminopyrimidine derivative of the formula (I-i), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 2,

wherein

R^2 is phenyl or naphthyl,

wherein

said phenyl and naphthyl are optionally having one or more substituents selected from the group consisting of halogen, amino, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, C_{1-6}alkylsulfonyl, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkyl substituted by cyano, hydroxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, or C_{1-6}alkoxy, C_{1-6}alkoxy, $N(R^{21})C(O)N(R^{22})(R^{23})$, and $N(R^{21})C(O)R^{24}$,

wherein

R^{21} is hydrogen or C_{1-6}alkyl;

R^{22} is C_{1-6}alkyl, or phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono- di-, or tri- halogen;

R^{23} is hydrogen or C_{1-6}alkyl; and

R^{24} is phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen.

4. The 2-aminopyrimidine derivative of the formula (I-i), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 2,

wherein

R^{11} and R^{12} independently represent hydrogen or methyl.

5. The 2-aminopyrimidine derivative of the formula (I-i), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 2, wherein said derivative is selected from the group consisting of the following compounds:

4-(3-aminopyrrolidin-1-yl)-6-phenylpyrimidin-2-amine trihydrochloride;

4-[3-(dimethylamino)pyrrolidin-1-yl]-6-phenylpyrimidin-2-amine trihydrochloride;

4-[3-(methylamino)pyrrolidin-1-yl]-6-phenylpyrimidin-2-amine trihydrochloride;

4-[3-(methylamino)pyrrolidin-1-yl]-6-(3-nitrophenyl)pyrimidin-2-amine trihydrochloride;

4-[(3R)-3-(methylamino)pyrrolidin-1-yl]-6-(3-nitrophenyl)pyrimidin-2-amine trihydrochloride;

4-[(3S)-3-(methylamino)pyrrolidin-1-yl]-6-(3-nitrophenyl)pyrimidin-2-amine trihydrochloride;

4-[(3S)-3-(methylamino)pyrrolidin-1-yl]-6-phenylpyrimidin-2-amine trihydrochloride;

4-[(3R)-3-(methylamino)pyrrolidin-1-yl]-6-phenylpyrimidin-2-amine trihydrochloride;

4-[3-(methylamino)pyrrolidin-1-yl]-6-(3-methylphenyl)pyrimidin-2-amine trihydrochloride;

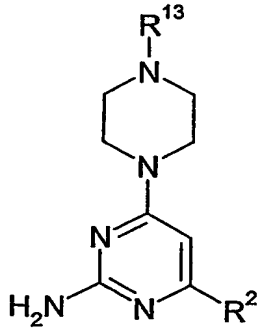
1-(3-{2-amino-6-[3-(methylamino)pyrrolidin-1-yl]pyrimidin-4-yl}phenyl)ethanone trihydrochloride;

3-{2-amino-6-[3-(methylamino)pyrrolidin-1-yl]pyrimidin-4-yl}phenol trihydrochlorid;

(3-{2-amino-6-[3-(methylamino)pyrrolidin-1-yl]pyrimidin-4-yl}phenyl)methanol trihydrochloride; and

3-{2-amino-6-[3-(methylamino)pyrrolidin-1-yl]pyrimidin-4-yl}benzonitrile trihydrochloride.

6. A 2-aminopyrimidine derivative of the formula (I-ii), its tautomeric or stereoisomeric form, or a salt,



(I-ii)

wherein

R^{13} is C_{1-6}alkyl optionally substituted by halogen, cyano, hydroxy, carboxy, amino, C_{1-6}-alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or C_{3-8}cycloalkyl; and

R^2 is phenyl having one or more substituents selected from the group consisting of carboxy, cyano, hydroxy, phenyl, C_{1-6}alkanoyl, N-(C_{1-6}alkyl)sulfonylamino, N-phenylsulfonylamino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, N-(C_{1-6}alkoxycabonyl)amino, N-arylamino, N-(aryl C_{1-6}alkyl)amino, aminocarbonyl, N-(C_{1-6}alkyl)aminocarbonyl, N,N-di(C_{1-6}alkyl)-aminocarbonyl, C_{3-8}cycloalkyl, C_{1-6}alkylsulfonyl, aryl C_{1-6}alkoxycarbonyl, C_{1-6}alkyl substituted by cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)-amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or mono-, di-, or tri- halogen, C_{1-6}alkoxy substituted by mono-, di-, or tri- halogen, $-N(R^{21})C(O)N(R^{22})(R^{23})$, and $N(R^{21})C(O)\ R^{24}$,

or

naphthyl optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, N-phenylsulfonylamino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)-amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, N-(C_{1-6}alkoxycabonyl)amino, N-arylamino, N-(aryl C_{1-6}alkyl)amino, aminocarbonyl, N-(C_{1-6}alkyl)aminocarbonyl, N,N-di(C_{1-6}-alkyl)aminocarbonyl, C_{3-8}cycloalkyl, C_{1-6}alkylsulfonyl, sulfamoyl, aryl C_{1-6}alkoxy-carbonyl, C_{1-6}alkyl optionally substituted by cyano, hydroxy, carboxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, C_{1-6}alkylthio, C_{1-6}alkoxy, or mono-, di-, or tri- halogen, C_{1-6}alkoxy optionally substituted by amono-, di-, or tri- halogen, $-N(R^{21})C(O)N(R^{22})(R^{23})$, and $N(R^{21})C(O)\ R^{24}$,

wherein

R^{21} is hydrogen or C_{1-6}alkyl;

R^{22} is C_{1-6}alkyl, or phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carbamoyl, cyano, hydroxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by mono-, di-, or tri- halogen;

R^{23} is hydrogen or C_{1-6}alkyl;

R^{24} is phenyl optionally having one or more substituents selected from the group consisting of halogen, amino, carboxy, carbamoyl, cyano, hy-

droxy, nitro, phenyl, C_{1-6}alkanoyl, C_{1-6}alkyl optionally substituted by hydroxy or mono-, di-, or tri- halogen, and C_{1-6}alkoxy optionally substituted by amono-, di-, or tri- halogen.

7. The 2-aminopyrimidine derivative of the formula (I-ii), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 6,

wherein

R^2 is phenyl having one or more substituents selected from the group consisting of cyano, phenyl, C_{1-6}alkanoyl, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylsulfonyl, trifluoromethyl, and C_{1-6}alkyl substituted by cyano, hydroxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, or C_{1-6}alkoxy,

or

naphthyl optionally having one or more substituents selected from the group consisting of cyano, hydroxy, phenyl, C_{1-6}alkanoyl, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, N-(C_{1-6}alkanoyl)amino, C_{1-6}alkoxycarbonyl, C_{1-6}alkylthio, C_{1-6}alkylsulfonyl, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkyl substituted by cyano, hydroxy, amino, C_{1-6}alkylamino, N,N-di(C_{1-6}alkyl)amino, or C_{1-6}alkoxy, and C_{1-6}alkoxy.

8. The 2-aminopyrimidine derivative of the formula (I-ii), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 6, wherein said derivative is selected from the group consisting of the following compounds:

3-[2-amino-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]phenol;

1-{3-[2-amino-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]phenyl}ethanone;

{3-[2-amino-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]phenyl}methanol;

4-(4-methylpiperazin-1-yl)-6-[3-(trifluoromethyl)phenyl]pyrimidin-2-amine;

4-biphenyl-3-yl-6-(4-methylpiperazin-1-yl)pyrimidin-2-amine trihydrochloride;

4-[3-(dimethylamino)phenyl]-6-(4-methylpiperazin-1-yl)pyrimidin-2-amine;

4-(4-methylpiperazin-1-yl)-6-(1-naphthyl)pyrimidin-2-amine; and

3-[2-amino-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl]benzonitrile.

9. A medicament comprising the 2-aminopyrimidine derivative, its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof as claimed in any one of claim 1 to 8 as an active ingredient.

10. The medicament as claimed in claim 9, further comprising one or more pharmaceutically acceptable excipients.

11. The medicament as claimed in claim 9, wherein said 2-aminopyrimidine derivative, its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof is a histamine H4 receptor antagonist.

12. The medicament as claimed in claim 9 for the treatment and/or prevention of an inflammatory disorder or disease.

13. The medicament as claimed in claim 12, wherein said inflammatory disorder or disease is asthma, rhinitis, allergic diseases or chronic obstructed pulmonary disease (CORD).

14. The medicament as claimed in claim 9 for the treatment and/or prevention of an immunological disorder or disease.

15. The medicament as claimed in claim 14, wherein said immunological disorder or disease is rheumatoid arthritis or atherosclerosis.

16. Use of a compound according to any one of claim 1 to 8 for manufacturing a medicament for the treatment and/or prevention of an inflammatory disorder or disease.

17. Use of a compound according to any one of claim 1 to 8 for manufacturing a medicament for the treatment and/or prevention of an immunological disorder or disease.

18. Process for controlling an inflammatory disorder or disease in humans and animals by administration of a histamine H4 receptor antagonisticly effective amount of a compound according to any one of claim 1 to 8.

19. Process for controlling an immunological disorder or disease in humans and animals by administration of a histamine H4 receptor antagonisticly effective amount of a compound according to any one of claim 1 to 8.